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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,155	10/14/2004	Oliver Schadt	MERCK-2932	9151
23599 7590 09/11/2007 MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			EXAMINER SHIAO, REI TSANG	
			ART UNIT 1626	PAPER NUMBER
			MAIL DATE 09/11/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/511,155

Applicant(s)

SCHADT ET AL.

Examiner

Rei-tsang Shiao, Ph.D.

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS; WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 9, 10, 12-16 and 18-22 is/are pending in the application.
- 4a) Of the above claim(s) 18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-10, 12-16 and 20-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

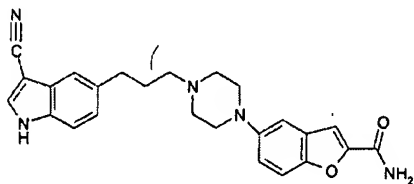
- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

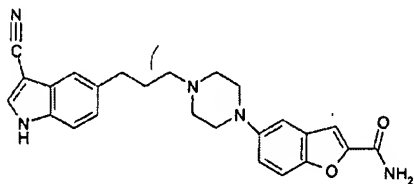
DETAILED ACTION

1. This application claims benefit of the foreign application: GERMANY 10217006.1 with a filing date 04/16/2002. However, an English-translated version of the foreign priority document has not been filed to the Office, the instant foreign priority has not been granted.
2. Amendment of claims 1-5, 9-10, 12-14, 18-20 and 22, cancellation of claims 8, 11, and 17 in the amendment filed on May 24, 2007, is acknowledged. Claims 1-7, 9-10, 12-16 and 18-22 are pending in the application.

Responses to Election/Restriction

3. Applicant's election with traverse of election of Group I claims 1-7, 9-10, 12-16 and 20-22, in part, in the reply filed on July 20, 2007 is acknowledged. Election of a single disclosed



species, i.e., , is also acknowledged. The traversal is on the grounds that it is earnestly submitted that the entirety of the present claims possess unity of invention under 37 C.F.R. §1.499. This is found persuasive, in part, and the reasons are given *infra*.

Claims 1-7, 9-10, 12-16 and 18-22 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-7, 9-10, 12-16 and 20-22, in part, drawn to compounds/compositions of formula (I), wherein the variable R^2 - R^5 independently does not contain a Het moiety (i.e., heterocyclic radical) thereof, the variables R^2 - R^5 independently is not substituted with a Het moiety (i.e., heterocyclic radical) thereof, the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof, when the variable Z represents an aromatic carbocyclic radical or heterocyclic radical and the heterocyclic radical is selected from the group consisting of thiophene, pyrrolyl, pyrazole, benzopyrane, benzofurane, benzodioxine, thiazole, benzothiadiazole, benzothiazole, pyridine, pyrimidine, indole, triazole, and quinoline thereof, their processes of making and methods of use (i.e., treating depression).

The claims 1-7, 9-10, 12-16 and 18-22 herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art, see Halazy et al. US 5,726,177. Chakravarty et al. disclose similar piperazine/indole compounds as the instant invention. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Furthermore, even if unity of invention under 37 CFR 1.475(a) is not lacking, which it is lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

- (1) A product and a process specially adapted for the manufacture of said product', or
- (2) A product and a process of use of said product; or

Art Unit: 1626

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

And, according to 37 CFR 1.475(c)

if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

However, it is noted that unity of invention is considered lacking under 37 CFR 1.475(a) and (b). Therefore, since the claims are drawn to more than a product, and according to 37 CFR 1.475 (e)

the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

The claims lack unity of invention and should be limited to only a product, or a process for the preparation, or a use of the said product. In the instant case, Groups I-IV are drawn to various products of formula (I)-(III), and the final products do not contain a common technical feature or structure, and do not define a contribution over the prior art, i.e., similar piperazine/indole compounds. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

Claims 1-7, 9-10, 12-16 and 20-22, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 1-7, 9-10, 12-16 and 20-22, in part, not embraced in above elected subject matter, and claims 18-19 are withdrawn from further

consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

The only direction or guidance present in the instant specification is the statement that instant compounds of formula (I) are 5HT reuptake-inhibiting and 5HT agonists, see lines 20-25 in the page 5. There are no *in vitro* or *in vivo* working examples present for the treatment of a disease mediated by 5-HT or inhibiting the activity of an excitatory amino acid in a cell by the administration of compounds of the instant invention.

Claim Rejections - 35 USC § 102

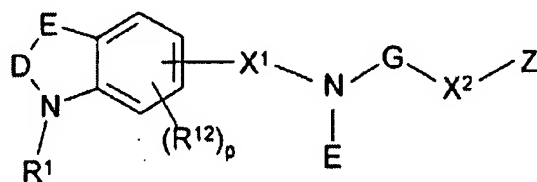
5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicants claims compound/compositions of formula (I), i.e.,



, wherein the variables E and G

together with the N atom to which they are bonded, are piperazine or piperidine thereof, and their processes of making and methods of use, see claim 1. Dependent claims 2-3, 5-7, 12-16 and 20-22 further limit a number of variable, i.e., Q is O.

5.1 Claims 1-3, 5-7, 12-16 and 20-22 are rejected under 35 U.S.C. 102(b) or as being anticipated by Halazy et al. US 5,726,177.

Halazy et al. disclose a number of compounds, see compounds No. 23-25, 35-43, 45 in columns 31-48. Halazy et al. compounds clearly anticipate the instant compounds of formula (I), wherein the variable E and G together with the N atom to which they are bonded, is piperazine, the variable Z represents an substituted aromatic carbocyclic radical (i.e., phenyl), the variable X¹ represents (CHR⁷)_h-Q-(CHR⁸)_k and the variable h is 0 and Q is O or C=O and k is 1 and R⁸ represents A and the variable A

Art Unit: 1626

represents alkyl(i.e., ethyl), R¹ represents H, D-E represents R²C=CR⁴ and R² or R⁴ independent represents (CH₂)_nN(R⁶) and n is 2 R⁶ is H, and X₂ is a bond.

5.2 Claims 1-3, 5-7, 12-16 and 20-22 are rejected under 35 U.S.C. 102(a) or as being anticipated by Bottcher et al. US 6,838,461.

Bottcher et al. disclose a number of compounds, see compounds of lines 1-25 in Column 11. Bottcher et al. compounds clearly anticipate the instant compounds of formula (I), wherein the variable E and G together with the N atom to which they are bonded, is piperazine, the variable Z represents an substituted aromatic carbocyclic radical (i.e., phenyl), the variable X₁ represents (CHR⁷)_h-Q-(CHR⁸)_k and the variable h is 0 and Q represents C=O and k is 0, and X₂ is (CHR⁷)_g and R⁷ represents A and A represents alkyl (i.e., ethyl) and the variable g is 1.

5.3 Claims 1-3, 5-7, 12-16 and 20-22 are rejected under 35 U.S.C. 102(a) or as being anticipated by Bottcher et al. US 6,723,725.

Bottcher et al. disclose a number of compounds, see compounds in Columns 10-11. Bottcher et al. compounds clearly anticipate the instant compounds of formula (I), wherein the variable E and G together with the N atom to which they are bonded, is piperazine, the variable Z represents an substituted aromatic carbocyclic radical (i.e., phenyl) or thiophene, D-E represents (CH₂)_nCO(CH₂)_mAr and n or m is 0, Ar is aromatic hydrocarbon radical (i.e., phenyl), the variable X₁ represents (CHR⁷)_h-Q-(CHR⁸)_k and the variable h is 0 and Q represents C=O and k is 0, and X₂ is

Art Unit: 1626

a bond or (CHR⁷)g and R⁷ represents A and A represents alkyl (i.e., ethyl) and the variable g is 1.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

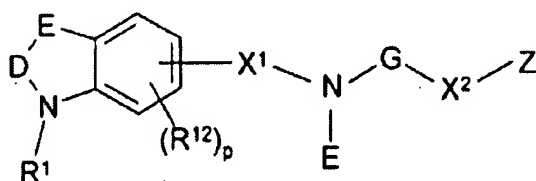
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Applicants claims compound/compositions of formula (I), i.e.,



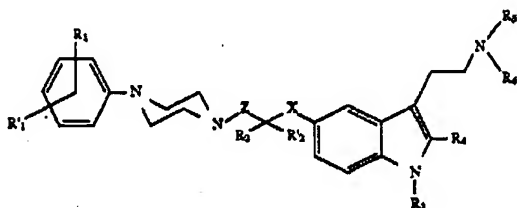
, wherein the variables E and G

together with the N atom to which they are bonded, are piperazine or piperidine thereof, and their processes of making and methods of use, see claim 1. Dependent claims 2-3, 5-7, 12-16 and 20-22 further limit a number of variable, i.e., Q is O.

6.1 Claims 1-7, 9-10, 12-16 and 20-22 are rejected under 35 U.S.C. 103(a) as being obvious over Halazy et al. US 5,726,177.

Determination of the scope and content of the prior art (MPEP §2141.01)

Halazy et al. disclose compound/composition of formula (I), i.e.,



, the variable Z represents C=O, or C=S, the

variable X represents CH₂ or O, see columns 2-3.

Determination of the difference between the prior art and the claims (MPEP

§2141.02)

The difference between the instant claims and Halazy et al. is that the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof, while Halazy et al. represents piperazine at the same position. Halazy et al. compounds/compositions overlap with the instant invention.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 1-7, 9-10, 12-16 and 20-22 prima facie obvious **because** one would be motivated to employ the compounds/compositions of Halazy et al. to obtain the instant compounds/composition of formula (I), wherein the variable R^2 - R^5 independently does not contain a Het moiety (i.e., heterocyclic radical) thereof, the variables R^2 - R^5 independently is not substituted with a Het moiety (i.e., heterocyclic radical) thereof, the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof.

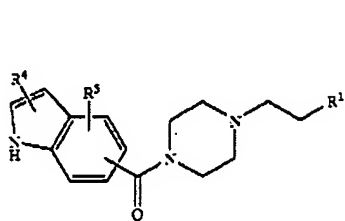
The motivation to obtain the claimed compounds/compositions derives from known Halazy et al. compounds would possess similar activities (i.e., 5-HT agonist or antagonists) to that which is claimed in the reference.

6.2 Claims 1-7, 9-10, 12-16 and 20-22 are rejected under 35 U.S.C. 103(a) as being obvious over Bottcher et al. US 6,838,461 or US 6,723,725.

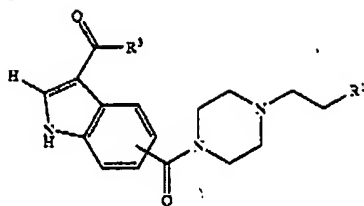
Determination of the scope and content of the prior art (MPEP §2141.01)

Bottcher et al. '461 or '725 independently disclose compound/composition of

formula (I), i.e.,



or



, see columns 1-2

respectively.

Determination of the difference between the prior art and the claims (MPEP

§2141.02)

The difference between the instant claims and Bottcher et al. '461 or '725 is that the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof, while Bottcher et al. '461 or '725 represents piperazine at the same position. Bottcher et al. compounds/compositions overlap with the instant invention.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 1-7, 9-10, 12-16 and 20-22 prima facie obvious **because** one would be motivated to employ the compounds/compositions of Bottcher et al. to obtain the instant compounds/ composition of formula (I), wherein the variable R²- R⁵ independently does not contain a Het moiety (i.e., heterocyclic radical) thereof, the variables R²- R⁵ independently is not substituted with a Het moiety (i.e., heterocyclic radical) thereof, the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof.

The motivation to obtain the claimed compounds/compositions derives from

known Bottcher et al. compounds would possess similar activities (i.e., 5-HT agonist or antagonists) to that which is claimed in the reference.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

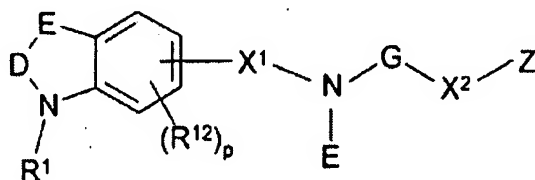
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-7, 9-10, 12-16 and 20-22 are rejected under the judicially created

Art Unit: 1626

doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 43 of Bottcher et al. US 6,838,461, or over claims 1 and 8 of Bottcher et al. US 6,723,725. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

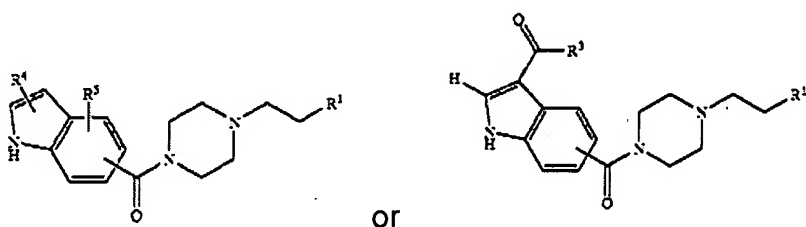
Applicants claims compound/compositions of formula (I), i.e.,



, wherein the variables E and G

together with the N atom to which they are bonded, are piperazine or piperidine thereof, and their processes of making and methods of use, see claim 1. Dependent claims 2-3, 5-7, 12-16 and 20-22 further limit a number of variable, i.e., Q is O.

Bottcher et al. '461 or '725 independently claim compound/composition of formula (I), i.e.,



, see columns 1-2

respectively.

The difference between the instant claims and Bottcher et al. '461 or '725 is that the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof, while Bottcher et al. '461 or '725 represents piperazine

Art Unit: 1626

at the same position. Bottcher et al. compounds/compositions overlap with the instant invention.

One having ordinary skill in the art would find the instant claims 1-7, 9-10, 12-16 and 20-22 *prima facie* obvious **because** one would be motivated to employ the compounds/compositions of Bottcher et al. to obtain the instant compounds/composition of formula (I), wherein the variable R^2 - R^5 independently does not contain a Het moiety (i.e., heterocyclic radical) thereof, the variables R^2 - R^5 independently is not substituted with a Het moiety (i.e., heterocyclic radical) thereof, the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof.

The motivation to obtain the claimed compounds/compositions derives from known Bottcher et al. compounds would possess similar activities (i.e., 5-HT agonist or antagonists) to that which is claimed in the reference.

Claim Objections

9. Claims 1-7, 9-10, 12-16 and 20-22 are objected to as containing non-elected subject matter, i.e., Het, benzoisothiazole, imidazole, pyrrolidine, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on pages 2-3 *supra*.

10. Claims 1 and 3 objected to because of the following informalities: In claim 1, line 10, recites the phrase "are, independently, ". Replacement of the phrase "are, independently, " with a phrase "are independently selected from" would obviate the objection. In claim 3, line 5, recite the phrase "are as defined above". Replacement of

the phrase "are as defined above " with a phrase "are as defined in claim 1" would obviate the objection.

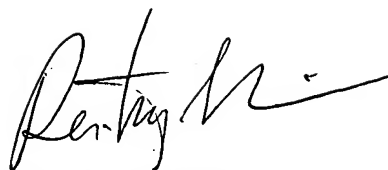
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Art Unit: 1626

A handwritten signature in black ink, appearing to read 'Rei-tsang Shiao', with a stylized flourish at the end.

Rei-tsang Shiao, Ph.D.
Patent Examiner
Art Unit 1626

September 06, 2007